REMARKS

Claims 31, 32, 43, 45-47, and 50-55 are pending in the application and under active consideration. Claim 44 has been canceled without prejudice or disclaimer. New claims 50-55 have been added. Claims 31, 32, and 43 have been amended. Entry of the amendments is respectfully requested.

Applicant has amended claim 31 to recite that the claimed MenB OS glycoconjugates has sialic acid residue N-acetyl groups replaced with N-C_3-C_8 acyl groups. Support for this amendment can be found in the specification, for example, at page 8, lines 1-11 and page 11, lines 1-7. Accordingly, the specification provides adequate support for this amendment.

Applicant has amended claim 32 to recite that the claimed MenB OS glycoconjugates has sialic acid residue N-acetyl groups replaced with saturated N-propionyl groups. Support for this amendment can be found in the specification, for example, at page 11, lines 8-11; and in Example 5 at page 34. Accordingly, the specification provides adequate support for this amendment.

In addition, claims 31, 32, and 43 have been variously amended as suggested by the Examiner to further clarify the intended subject matter of the claimed invention. These amendments to the claims are made solely to obtain expeditious allowance of the instant application and not for reasons related to patentability.

New claims 50-55 have been added. Support for the new claims can be found in the original claims and throughout the specification, for example, at pages 10-14 and page 17, line 25 through page 18, line 13.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicant expressly reserves the right to file one or more continuing applications hereof containing the canceled or unamended claims.

Double Patenting Rejection

Claims 31, 32, and 43-47 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent

No. 6,638,513. Applicant reiterates the request that the requirement for submission of a Terminal Disclaimer with respect to U.S. Patent No. 6,638,513 be held in abeyance until there is an indication of allowable subject matter in the present application.

Rejection under 35 U.S.C. § 103

Claims 31, 32, and 43-47 are rejected under 35 U.S.C. § 103 as being unpatentable over the reference of Jennings et al. U.S. Patent No. 5,811,102 in view of the references of Sato et al. (1995) J. Biol. Chem. 270:18923-18928 and Staveski et al. U.S. Patent No. 5,354,853. The rejection under 35 U.S.C. § 103 is maintained on the grounds that Applicant allegedly "has provided no evidence within the instant specification to demonstrate that the claimed glycoconjugate differs in any unexpected or unobvious manner from that which one of ordinary skill in the art would have expected to obtain upon combining the teachings of the cited references" (Office Action, page 6). Applicant respectfully traverses the rejection for the reasons already made of record in the response to the Office Action of September 30, 2004 and on the following grounds.

The reference of Jennings et al. fails to teach or suggest MenB OS in which sialic acid residue N-acetyl groups have been replaced with N-C_3-C_8 acyl groups where the MenB OS has an average degree of polymerization of 10-20. The Examiner points out that Jennings et al. disclosed MenB OS glycoconjugates in which "[t]he average molecular weight of the MenB oligosaccharide derivative was about 10 to 200 sialic acid residues (see column 5, lines 32-35), which encompasses the MenB OS having an average Dp of about 12 to 18, or 10 to 20 recited in the instant claims" (Office Action, page 9). However, Jennings et al. fail to disclose or suggest a conjugate having a substantially homogenous sized group of MenB OS. The attention of the Examiner is directed to Figures 1-4 depicting the claimed glycoconjugates of the invention. Applicant respectfully points out that the glycoconjugates comprise multiple saccharide chains attached to a carrier. The glycoconjugate described by Jennings et al. is formed from a heterogeneous population of MenB polysaccharide and comprises a carrier molecule with multiple polysaccharide chains, which on average are longer and more varied in length

than those of the instant invention. Thus, the glycoconjugate described by Jennings et al. has a different structure.

Moreover, the conjugates of the instant invention differ from those described by Jennings et al. because they are produced by a different process. Applicant has added the step of "obtaining a substantially homogenous sized group of MenB OS." See specification, for example, at page 11, line 25 through page 12, line 19, which describes fragmenting the MenB polysaccharide and size fractionation of the resulting oligosaccharide fragments to produce a homogeneous population of MenB oligosaccharides having the specified degree of polymerization. Although, the process of acylating sialic acid residues and conjugation of MenB polysaccharide to a carrier molecule, described by Jennings et al., may be accompanied by minor degradation of the polysaccharide, the derivitization process does not produce a population of oligosaccharides with a degree of polymerization of 12 to 18 or 10 to 20, as claimed in the instant application. Applicant has found that unsized MenB polysaccharide that has not been treated with a fragmentation step typically has an average degree of polymerization of greater than 30 (see specification, for example, at page 28, lines 1-4). In addition, the saccharide to protein ratio in glycoconjugates differs depending on the method used to form the glycoconjugate. Measurements of the saccharide to protein ratios for MenB glycoconjugates indicate that the preparation of a glycoconjugate from a homogeneous sized population of MenB OS improves the coupling efficiency of saccharide antigens to the protein carrier (see specification, for example at page 36, lines 25-35). Thus, the claimed glycoconjugates produced by the process described in the instant application are structurally distinct from the glycoconjugates described by Jennings et al.

Moreover, Applicant foresees that glycoconjugates comprising a more homogeneous population of MenB OS may have the advantage of exhibiting more consistent immunological behavior than glycoconjugates comprising a heterogenous MenB polysaccharide (see specification for example, at page 37, lines 6-11). Jennings et al. fails to provide any motivation for using a homogenous sized population of MenB OS.

Thus, the reference of Jennings et al. fails to teach or suggest the precisely claimed glycoconjugates of the instant invention.

Furthermore, claim 32, is not obvious in view of the cited references. As currently amended, claim 32 recites MenB OS in which sialic acid residue N-acetyl groups have been replaced with saturated N-propionyl groups. The reference of Jennings et al., in contrast, clearly refers to MenB polysaccharides in which sialic acid residue N-acetyl groups have been replaced with unsaturated N-acyl derivative polysaccharides (see *e.g.*, column 5). Thus, the reference of Jennings et al. fails to describe or suggest saturated N-propionylated MenB OS that is substantially homogenous sized with the specified degree of polymerization as claimed in the present invention. Thus, Applicant, again, has disclosed and claimed MenB OS glycoconjugates that contain recited elements not disclosed by Jennings et al.

Jennings et al. also fails to teach or suggest a glycoconjugate comprising a covalently attached C3-C16 long-chain aliphatic lipid. The secondary references of Sato et al. and Staveski et al. do not cure the deficiencies of Jennings et al. as neither reference discloses the claimed glycoconjugates comprising homogeneous sized MenB OS in which sialic acid residue N-acetyl groups are replaced with N-C_3-C_8 acyl groups. The reference of Sato et al. describes some saccharide-lipid conjugates; however, the saccharides used in the conjugates are structurally different from the MenB OS with N-C_3-C_8 acyl groups described in the instant application. Sato et al. fails to describe or suggest glycoconjugates comprising MenB OS, nor provides any incentive for using MenB OS. The reference of Staveski et al. discloses phospholipid-saccharide conjugates and their use to produce liposomes, but also fails to teach or suggest the claimed MenB OS with N-C_3-C_8 acyl groups, nor provides any incentive to use the claimed MenB OS glycoconjugates.

Therefore, the references do not disclose or suggest all the limitations of the present invention, and the Examiner has not met the burden of establishing a *prima facie* case of obviousness. For at least the above reasons, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

New Matter Rejection under 35 U.S.C. § 112, first paragraph

Claim 31 has been rejected under 35 U.S.C. § 112, first paragraph on the grounds that the previous amendment of the claim introduced limitations that are allegedly new matter. In particular, the Office Action alleges that "the scope of the terms 'N-acyl groups' and 'a carrier molecule' is not the same as the scope of the terms 'N-propionyl groups' and 'a protein carrier' respectively" (Office Action, page 7).

As currently amended, claim 31 recites that the claimed glycoconjugate is produced by a method including the steps of "providing a heterogenous population of *Neisseria meningitidis* serogroup B capsular oligosaccharide (MenB OS) in which sialic acid residue N-acetyl groups are replaced with N-C_3-C_8 acyl groups" and "covalently attaching the single end-activated MenB OS to a protein carrier molecule." These recitations are adequately supported in the application as filed. See the specification, for example, at page 8, lines 1-11; page 11, lines 1-7; page 13, lines 26-34; and page 16, lines 1-22. Applicant notes that the preparation of the N-propionyl derivative is merely described as a preferred embodiment, and not as the only embodiment. Limiting the invention to the propionyl derivative depicted in the figures and described in the examples of the specification would improperly limit the claims to the preferred embodiment. See, *e.g.*, *Karlin Technology, Inc. v. Surgical Dynamics, Inc.*, 50 USPQ2d 1465 (Fed. Cir. 1999).

Therefore, withdrawal of the new matter rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 31, 32, and 43-47 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." (Office Action, pages 8-9).

(a) The Examiner alleges that "[c]laim 31 is indefinite, confusing, and internally inconsistent in terms of scope, in the recitations 'A glycoconjugate produced by a

method' in line 1 of the claim and 'to provide a MenB OS glycoconjugate' at the end of the claim." In particular, the Office Action points out that "[w]hat is obtained at the end of step (d) of the recited method is not a generic 'glycoconjugate', but a specific MenB OS glycoconjugate." (Office Action, page 8). In order to expedite prosecution, Applicant has amended claim 31 as suggested by the Examiner to replace the limitation in line 1 of the claim with "a substantially homogenous sized *Neisseria meningitidis* serogroup B capsular oligosaccharide (MenB OS) produced by a method." In addition, part (a) of the claim now recites "providing a heterogenous population of MenB OS in which sialic acid residue N-acetyl groups are replaced with N-C_3-C_8 acyl groups;" and part (e) of the claim now recites "covalently attaching the single end-activated MenB OS to a protein carrier molecule to provide the substantially homogenous sized MenB OS glycoconjugate."

(b) Claim 32 has been amended similarly to claim 31.

(c) The Examiner alleges that "[c]laims 31 and 32 are vague, indefinite and confusing in the recitation 'the MenB OS' in step (c) of the claims, because it is unclear which 'MenB OS' provides antecedent basis for the limitation" (Office Action, page 8). In order to expedite prosecution, part (c) of claim 31 has been amended to recite "covalently attaching a C3-C16 long-chain aliphatic lipid to the nonreducing end of the MenB OS obtained in step (b)."

(d) The Examiner alleges that "[i]n step (d) of claims 31 and 32, for proper antecedent basis, it is suggested that Applicants replace the limitation 'single end-activated MenB OS' with the limitation --single end-activated MenB OS of said DP--" (Office Action, page 8). In order to expedite prosecution, step (d) of claims 31 and 32 have been amended as suggested by the Examiner to recite "single end-activated MenB OS of said DP."

(e) The Examiner alleges that "[c]laim 43, which depends from claim 31, is confusing, incorrect and/or has improper antecedence in the limitation: 'the reactive

group introduced in step (c)', because step (c) of claim 31 does not recite any 'reactive group' (Office Action, page 8). Applicant has amended claim 43 to recite the "reactive group introduced in step (d)" to correct antecedent basis.

(f) Claims 43-47 which depend directly or indirectly from claim 31, are also rejected as allegedly being indefinite "because of the indefiniteness or vagueness identified above in the base claim" (Office Action, page 9). Applicant respectfully traverses the rejection on this basis for at least the reasons stated above.

For at least the above reasons, Applicant respectfully requests that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

CONCLUSION

In light of the above remarks, Applicant submits that the present application is fully in condition for allowance. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicant invites the Examiner to contact the undersigned.

The Commissioner is hereby authorized to charge any fees and credit any overpayment of fees which may be required under 37 C.F.R. §1.16, §1.17, or §1.21, to Deposit Account No. 18-1648.

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